Does PET scan have any role in the diagnosis of perineural spread associated with the head and neck tumors?

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Abstract

Background. Perineural spread of head and neck tumors is linked to a worse chance of survival as well as a higher risk of local recurrence and metastasis. Particle emission tomography/computed tomography (PET/CT) using 2-[fluorine-18]fluoro-2-deoxy-d-glucose (FDG) is part of the work-up and follow-up of many afflicted patients, and radiologists play an essential role in the assessment and management of head and neck cancer.

Objectives. The purpose of the current study was to investigate the diagnostic performance of ^{18}F-FDG PET in detecting perineural spread among patients with head and neck tumors through a meta-analysis.

Materials and methods. Relevant articles were searched using appropriate keywords from PubMed, MEDLINE and PubMed Central (PMC) databases. Retrospective and prospective studies were included as per the predefined PICOS criteria. Demographic summary and event data for diagnostic accuracy of ^{18}F-FDG PET were determined, and odds ratio (OR), sensitivity, specificity, likelihood ratios, and predictive values were calculated using RevMan software. The bias risk was analyzed with Egger's and Begg's tests using MedCalc software.

Results. Fourteen clinical trials performed between 2000 and 2021, with 977 head and neck cancer patients with perineural spread, were included according to the inclusion criteria. Included studies used ^{18}F-FDG PET imaging of tumors and reported its high sensitivity. In the current study, we obtained the pooled OR = 3.088 (95% confidence interval (95% CI): [1.486; 6.419]), pooled sensitivity of 91.7%, pooled specificity of 92.35%, positive predictive value (PPV) of 92.27%, negative predictive value (NPV) of 91.13%, positive likelihood ratio of 7.45, negative likelihood ratio of 0.28, disease prevalence of 95.8%, and accuracy of 91.5%. Data was heterogeneous, with Q value of 33.8%, degrees of freedom (df) value of 13, I^2 value of 61.5% (31.23–78.5), and p-value = 0.0013. The risk of publication bias was low, with a p = 0.7490 (Egger's test) and p = 0.7843 (Begg's test).

Conclusions. The present meta-analysis highly recommends ^{18}F-FDG PET as an effective imaging method for patients with head and neck tumors with perineural spread.

Key words: MRI, head and neck tumors, perineural spread, perineural invasion, FDG PET scan

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Background

The concept of 'head and neck cancer' refers to a diverse class of cancers that affect the oral cavity, pharynx, larynx, nasal cavity, paranasal sinuses, and salivary glands. Head and neck cancer has several histologic subtypes due to the large array of structures and cell types.[1]

Head and neck tumors can spread through several processes, including direct extension, hematogenous dissemination and lymphatic dissemination. Furthermore, a phenomenon known as perineural spread allows some cancers to exploit peripheral nerves as a direct conduit for tumor development, away from the initial location. Perineural spread is important in clinical practice because it indicates a poor prognosis, even asymptomatic. Furthermore, it is frequently overlooked during surgery and can develop without hematogenous or lymphatic metastases.[2]

In the literature, the words 'perineural invasion' and 'perineural spread' are frequently used interchangeably; thus, it is vital to distinguish between them.

Perineural spread can affect any cranial nerve and its branches. However, the trigeminal nerve (cranial nerve V) and the facial nerve (cranial nerve VII) are the most afflicted, owing to their extensive innervation of the head and neck tissues. In addition, the perineural spread is more likely in tumors that are located in the midface, in men, in larger tumors, in recurrence after therapy, and in tumors with poor histologic distinction.[3]

Perineural invasion is a histologic diagnosis that is difficult to establish with macroscopic imaging modalities. However, the perineural spread spreads tumor cells along a nerve and such infiltration may be seen with imaging tools. Therefore, the radiologist must determine whether a tumor that is directly next to a nerve is considered a perineural spread or not.

The perineural spread has an adverse impact on the treatment outcome with a poor prognosis. The long-term survival is jeopardized. Previous studies have reported that unrecognized perineural tumor invasion leads to treatment failure. Henceforth, it is necessary to detect and accurately diagnose such spread.[4,5]

Imaging is widely known to have an essential role in diagnosis and treatment of head and neck cancers. The frequently used imaging methods for detecting perineural spread are magnetic resonance imaging (MRI), computed tomography (CT) and positron emission tomography (PET) scan, among others. Among these, the use of ^{18}F-FDG PET (PET with 2-[fluorine-18]fluoro-2-deoxy-d-glucose (FDG)) is highly recommended in various studies due to its high sensitivity for detecting perineural spread and recurrent metastatic tumors.[6–20] For example, Schroeder et al. reported that MRI and ^{18}F-FDG PET have identical detection rates of recurrent metastatic tumors.[16] Similarly, Lee et al. reported that the application of ^{18}F-FDG PET in clinical diagnosis could enhance the tumor detection rate in head and neck cancers.[20]

In contrast to these studies, Hanna et al. concluded that MRI has higher sensitivity and specificity for perineural spread and malignant tumor detection.[21] These contrasting reports limited the use of ^{18}F-FDG PET as an effective diagnostic tool. Therefore, the current meta-analysis aimed to statistically analyze the available literature related to ^{18}F-FDG PET and predict its diagnostic accuracy.

Objective

This study aims to investigate the diagnostic performance of ^{18}F-FDG PET in determining perineural spread in patients with head and neck tumors.

Materials and methods

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) normative recommendations in this study with the PROSPERO registration No. CRD42021244688. All procedures performed in the study were in accordance with the institutional and/or national research standards set by the Ethics Committee of the Shandong University (Jinan, China), and with the 1964 Helsinki Declaration and its later amendments, or comparable ethical standards.

Search strategy

This meta-analysis is based on an extensive search conducted in databases of MEDLINE (through PubMed), Cinahl (through EBSCO), Scopus, and Web of Sciences. The following keywords were used for searching the relevant studies: [^{18}F-FDG PET], [perineural spread], [head and neck cancer], [CT scan], and [MRI]. All the included articles were selected as per the predefined PICOS criteria and PRISMA guidelines, and studies were selected randomly, irrespective of the language, publication status or type of study (prospective, retrospective, clinical trial). Demographic summary of the patients and event data of the included studies are summarized in Table 1.[6–19] Two authors (XN and JZ) scanned the relevant sources for related studies separately. Mainly, the full-texts articles of the sources were collected, and abstracts were used to obtain sufficient information for the meta-analysis. Obsolete references were excluded, and valuable studies were included as per the inclusion criteria. Then, event data with useful variables were collected by 2 researchers (ZJ and JS) independently.

Inclusion and exclusion criteria

The studies included in the meta-analysis reported the use of ^{18}F-FDG PET as an effective imaging method for diagnosing patients with head and neck tumors with perineural spread, and were published between 2000 and 2021. Only the full-text data were included in the current study, while studies with insufficient data, studies reporting the use

Table 1. Demographic summary of the studies

Study and year	Total samples studied	Type of study	Age of patients [years]	Duration	Gender (M/F)	Instrument detail
Ng et al. 2005[6]	151	prospective	26–82	2 weeks	121 M/3 F	PET system (ECAT EXACT HR; Siemens/CTI, Knoxville, USA)
Schöder et al. 2006[7]	142	prospective	37–84	2 years 2 months	21 M/10 F	Integrated PET/CT scanner: Biograph (Siemens) or Discovery LS (GE Healthcare, Milwaukee, USA)
Kim et al. 2007[8]	64	retrospective	60	1 year	267 M/82 F	Biograph Sensation16 scanner (Siemens/CTI)
Gu et al. 2010[9]	46	retrospective	39–89	2 weeks	39 M/7 F	Discovery STE Whole Body PET/CT System (GE Healthcare)
El-Khodary et al. 2011[10]	38	retrospective	58	3 years 2 months	51 M/12 F	Discovery STE 16 (GE Healthcare)
Pereira et al. 2012[11]	49	retrospective	36–81	4 years	44 M/5 F	Siemens Biograph Integrated PET/CT scanner (Siemens/CTI)
Karapolat and Kumanlıoğlu 2012[12]	20	retrospective	20–76	3 years 2 months	19 M/1 F	Siemens HI-REZ Biograph 6 (Siemens/CTI)
Gődény et al. 2016[13]	38	retrospective	24–78	4 years	24 M/14 F	3T wide-bore MR scanner (General Electric Discovery 750w; GE Healthcare)
Ceylan et al. 2018[14]	22	retrospective	18–89	1 year 10 months	49 M/16 F	Siemens Biograph 16 TruePoint PET/CT scanner (Siemens/CTI)
Sherif et al. 2018[15]	50	retrospective	17–74	1 year	34 M/16 F	PET/CT scanner (Gemini TF; Philips, Andover, USA) with multislice-16 scanner
Schroeder et al. 2020[16]	25	retrospective	49–79	4 years	17 M/8 F	Integrated PET/CT system (Biograph mCT 128 True V; Siemens/CTI)
Park et al. 2020[17]	134	retrospective	47–83	9 months	48 M/25 F	PET/MRI system (Biograph mMR; Siemens Healthcare, Erlangen, Germany)
Sarma et al. 2021[18]	63	retrospective	32–83	8 years	55 M/8 F	General Electric Discovery PET 8 slice CT scanner (GE Healthcare)
Linz et al. 2021[19]	135	prospective	23–88	2 years 6 months	74 M/61 F	PET/CT scanner (Siemens Biograph mCT 64; Siemens Healthcare)

M – male; F – female; PET/CT – particle emission tomography/computed tomography.

of other imaging methods, and all studies published before 2000 were excluded, as shown in Fig. 1.

Evaluation of the analytical standard and source of heterogeneity

Two reviewers (XN and JZ) separately evaluated the methodological validity of the included studies and calculated the heterogeneity in the included experiments. At the same time, one author (WC) was responsible for resolving disagreements between authors (XN and JZ). In order to investigate the heterogeneity, Cochran's Q statistic and I^2 index in the random bivariate model were calculated with the help of RevMan software v. 5 (The Cochrane Collaboration, The Nordic Cochrane Center, Copenhagen, Denmark). The investigated heterogeneity sources were the use of full-text publication compared to abstracts, prospective compared to retrospective studies, different numbers of patients with diverse types of head and neck cancers, and different imaging instruments.

Statistical analyses

The DerSimonian–Laird technique calculated the diagnostic odds ratio (OR) for statistical analysis. A 2 × 2 table was made using the event data, and meta-analysis was performed using RevMan and MedCalc v. 20.100 (MedCalc Software, Ostend, Belgium) software. Pooled diagnostic OR with 95% confidence intervals (95% CIs), respective forest plot, heterogeneity of studies (in terms of Q value, degrees of freedom (df) value, I^2 value, and p-value), pooled sensitivity, specificity, likelihood ratios, predictive values, disease prevalence, accuracy, and receiver operating characteristic (ROC) analysis were performed with the help of MedCalc software. In addition, Deeks' funnel plot for publication bias, Youden plot to assess investigation error, and hierarchical summary receiver operating characteristic (HSROC) curve were created using MedCalc software, while forest plot of sensitivity and specificity was plotted using RevMan software.

Results

Literature search results

We found a total of 1246 studies in different databases, and excluded 227 studies after reading their titles and abstracts; as a result, 1019 records were screened. Further, due to invalid references and duplicity, we excluded 784 studies and included only 235 studies for the final

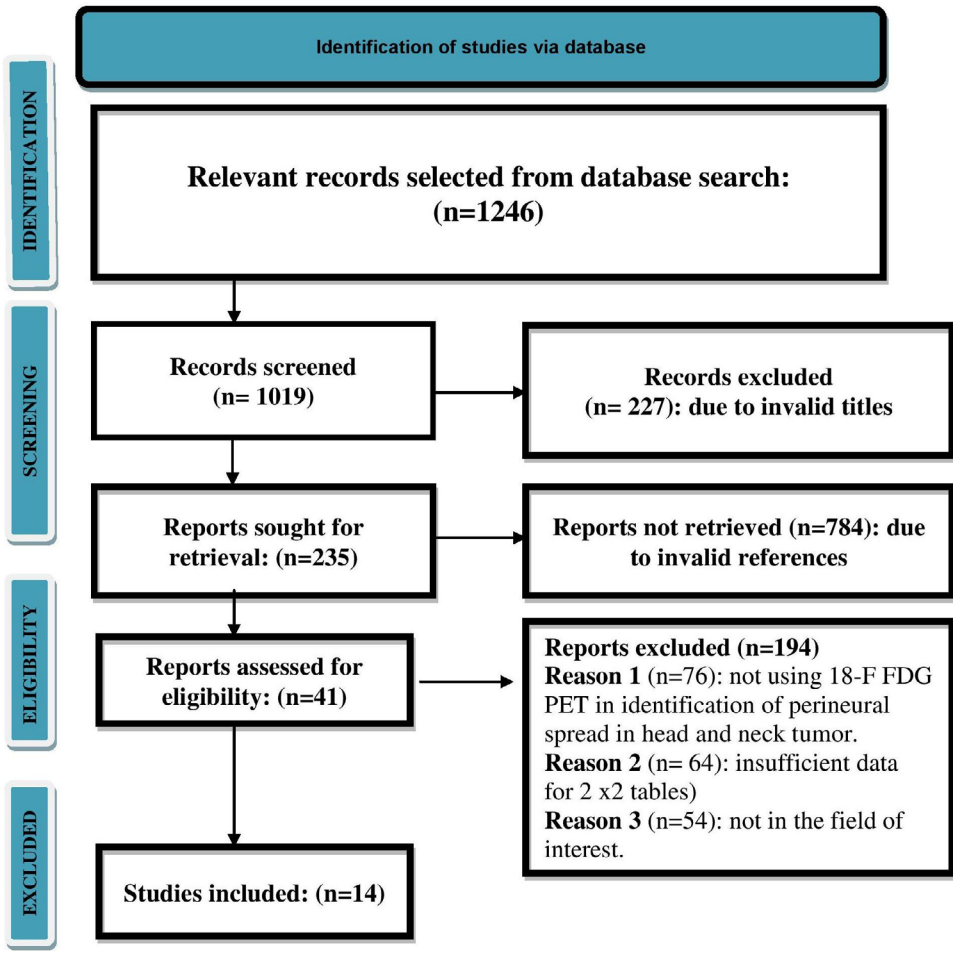

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of the study group

screening. Out of these 235 studies, 194 studies were excluded based on the inclusion criteria, and eligibility of the remaining 41 studies was assessed further. The critical reasons for omission were inadequate evidence and inappropriate comparison criteria to create 2 × 2 tables for review. Finally, 14 studies from 2000–2021 which fulfilled the inclusion criteria, i.e., ^{18}F-FDG-PET for detection of perineural spread in head and neck tumor patients, were subject to meta-analysis, as shown in Fig. 1. Those 14 studies included a total of 977 head and neck tumor patients of different age groups, chosen randomly and scanned with ^{18}F-FDG PET and CT or MRI. The demographic details of the studies included in this meta-analysis are shown in Table 1 – the author of the study, publishing year, duration of the study, type of study, total sample size, age of patients, gender of patients, and type of instrument used. In addition, event data of these studies (including the number of total samples studied, a true positive result, true negative result, false negative result, and false positive results) were collected.

Meta-analysis results

The risk of bias for included studies was assessed as shown in Table 2, and publication bias was measured with the help of Egger's test, Begg's test and Deeks' funnel plot. The current meta-analysis has a low risk of publication bias, as apparent from the funnel plot (Fig. 2), since p-values of both tests are greater than 0.05 (p-value of Egger's test = 0.7490 and p-value of Begg's test = 0.7843).

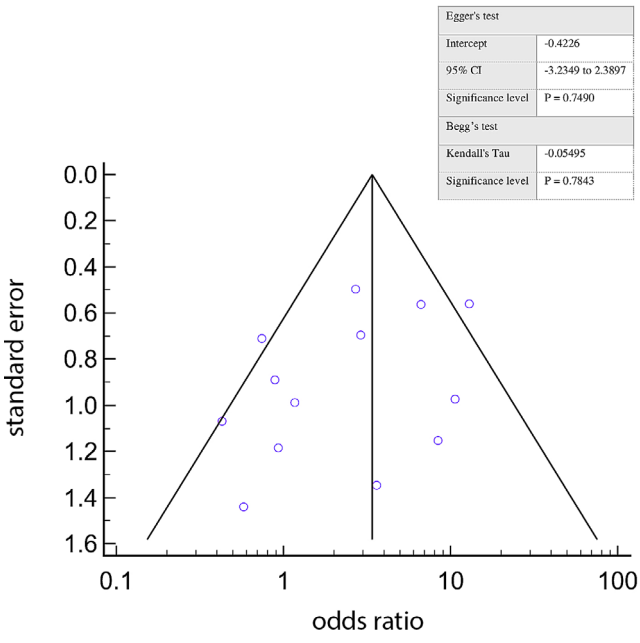

Fig. 2. Funnel plot for publication bias

95% CI – 95% confidence interval.

Table 2. Risk assessment for included studies

Variable	Ng et al. 2005[6]	Schöder et al. 2006[7]	Kim et al. 2007[8]	Gu et al. 2010[9]	El-Khodary et al. 2011[10]	Pereira et al. 2012[11]	Karapolat and Kumanlıoğlu 2012[12]	Gödény et al. 2016[13]	Ceylan et al. 2018[14]	Sherif et al. 2018[15]	Schroeder et al. 2020[16]	Park et al. 2020[17]	Sarma et al. 2021[18]	Linz et al. 2021[19]
Type of study	P	P	R	R	R	R	R	R	R	R	R	R	R	P
Was a consecutive or random sample of patients enrolled?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Did the study avoid inappropriate exclusions?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were all patients included in the analysis?	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Was the target population having patients of different age groups and included both genders?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were study participants sampled in an appropriate way?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were the study subjects and the setting described in detail?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were valid methods used for the identification of the condition?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the condition measured in a standard, reliable way for all participants?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was there appropriate statistical analysis conducted?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

P – prospective; R – retrospective; Y – yes; N – no.

The OR of the included studies was calculated using MedCalc software, and the respective forest plot was created (Fig. 3). We obtained the pooled OR value of 3.088 with 95% CI of [1.486; 6.419]. Data used for this analysis were heterogeneous, and we achieved the Q value of 33.8%, df value of 13, I^2 value of 61.5% (31.23–78.5),

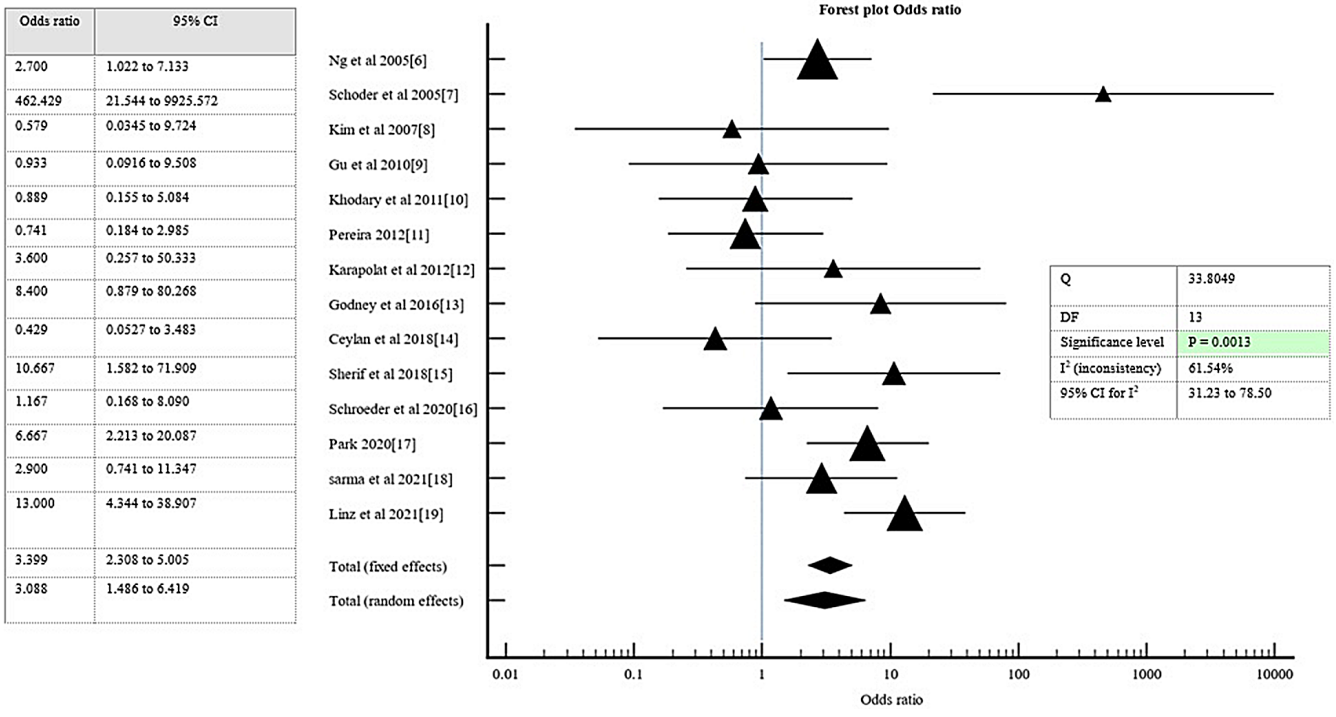

Fig. 3. Forest plot for diagnostic odds ratio

95% CI – 95% confidence interval; df – degrees of freedom.

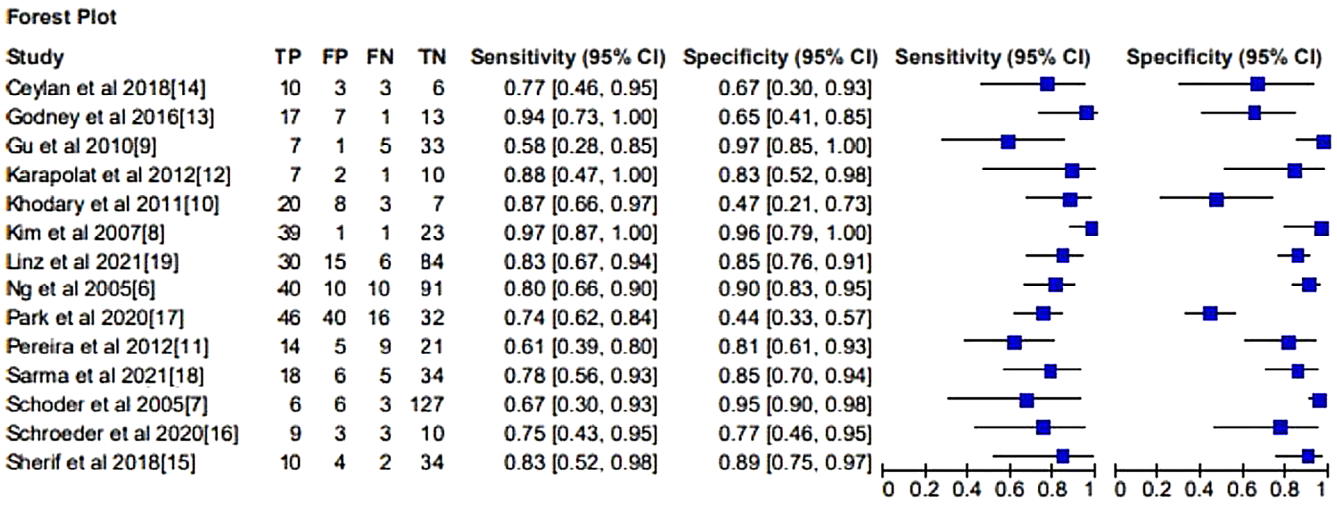

Fig. 4. Forest plot for sensitivity and specificity

95% CI – 95% confidence interval; TP – true positive; FP – false positive; FN – false negative; TN – true negative.

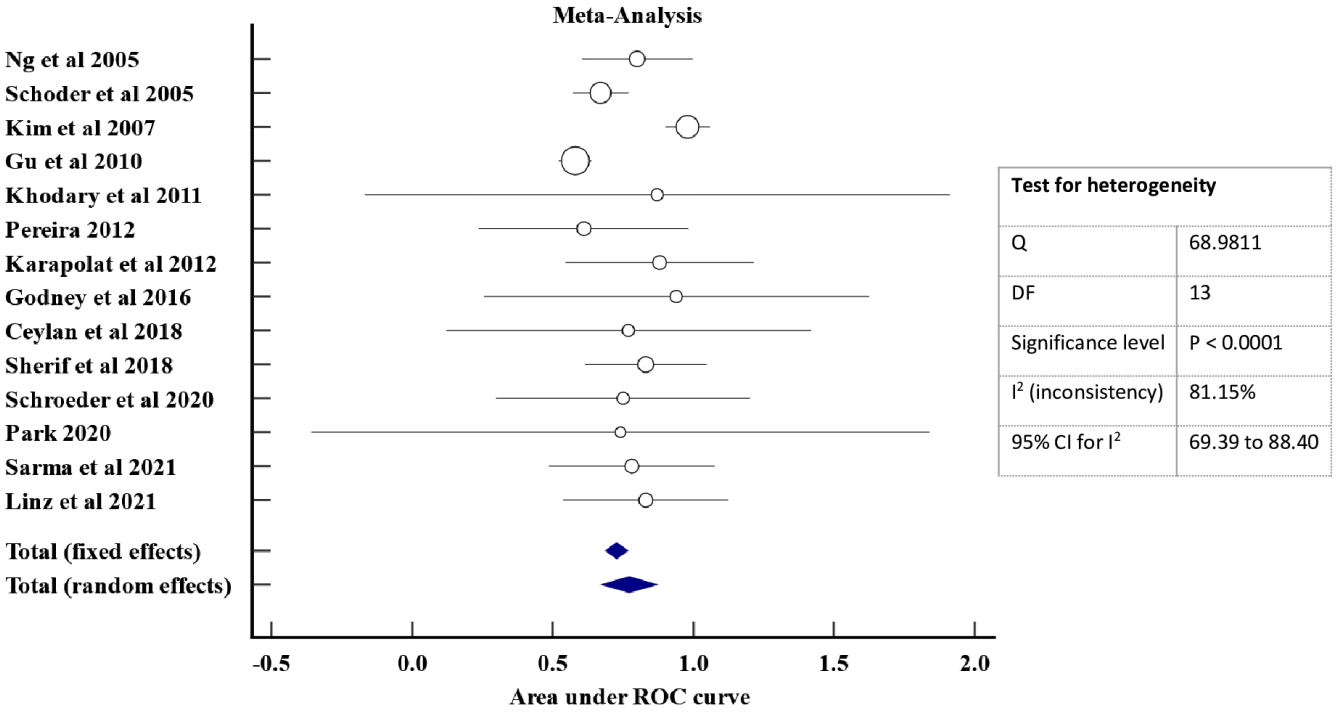

Fig. 5. Forest plot area under receiver operating characteristic (ROC) curve (area under the curve (AUC)

95% CI – 95% confidence interval; df – degrees of freedom.

and p-value of 0.0013. We obtained the pooled sensitivity of 91.7%, pooled specificity of 92.35%, positive predictive value (PPV) of 92.27%, negative predictive value (NPV) of 91.13%, the positive likelihood ratio of 7.45, negative likelihood ratio of 0.28, disease prevalence of 95.8%, and accuracy of 91.5%, as reported in Table 3. All of these results are statistically significant. The forest plot of sensitivity and specificity was designed using RevMan software, as shown in Fig. 4.

The ROC analysis was performed using MedCalc software, a forest plot was designed as shown in Fig. 5 and heterogeneity was assessed. The included data were heterogeneous, as we obtained the Q value of 68.9%, df value of 13, I^2 consistency of 81.15% with 95% CI of [69.39; 88.40], and significance level (p-value) of 0.0001. In order to assess the study errors, the Youden curve was plotted between PPV and NPV (Fig. 6), and we found that the included studies have minimum investigations error. The HSROC curve was also plotted between the sensitivity and specificity of included studies (Fig. 7). All these curves and results are statistically significant and reflect the high sensitivity and specificity of ^{18}F-FDG PET, as an effective imaging method for detecting perineural spread in patients of head and neck tumors.

Table 3. Statistical summary of the included studies: 95% CI – 95% confidence interval.

Study ID	Sensitivity [%] [95% CI]	Specificity [%] [95% CI]	PLR [95% CI]	NLR [95% CI]	Disease prevalence [%] [95% CI]	PPV [95% CI]	NPV [95% CI]	Accuracy [%] [95% CI]
Ng et al. 2005[6]	80 [66.28; 89.97]	90.09 [82.54; 95.15]	8.08 [4.41; 14.79]	0.22 [0.13; 0.39]	33.11 [25.68; 41.23]	80 [68.61; 87.98]	90.10 [83.89; 94.08]	86.75 [80.29; 91.72]
Schöder et al. 2006[7]	66.7 [29.93; 92.51]	95.48 [90.44; 98.33]	14.77 [5.96; 36.65]	0.34 [0.14; 0.88]	6.34 [2.94; 11.69]	50 [28.74; 71.26]	97.69 [94.38; 99.07]	93.66 [88.31; 97.06]
Kim et al. 2007[8]	97.5 [86.84; 99.94]	95.83 [78.88; 99.89]	23.4 [3.43; 159.51]	0.02 [0.00; 0.18]	62.50 [49.51; 74.30]	97.5 [85.12; 99.63]	95.83 [76.82; 99.38]	96.87 [89.16; 99.62]
Gu et al. 2010[9]	58.3 [27.67; 84.83]	97.05 [84.67; 99.93]	19.83 [2.71; 144.99]	0.42 [0.22; 0.84]	26.09 [14.27; 41.13]	87.5 [77.12; 92.82]	86.84 [77.12; 92.82]	86.95 [73.74; 95.06]
El-Khodary et al. 2011[10]	86.9 [66.41; 97.22]	46.66 [21.27; 73.41]	1.63 [0.99; 2.69]	0.27 [0.09; 0.91]	60.53 [43.39; 75.96]	71.43 [60.28; 80.46]	70.00 [41.62; 88.42]	71.05 [54.10; 84.58]
Pereira et al. 2012[11]	60.86 [38.54; 80.29]	80.76 [60.65; 93.45]	3.16 [1.35; 7.43]	0.48 [0.28; 0.83]	46.94 [32.53; 61.73]	73.68 [54.4; 86.79]	70.00 [57.55; 80.07]	71.42 [56.74; 83.42]
Karapolat and Kumanlıoğlu et al. 2012[12]	87.5 [47.35; 99.68]	83.33 [51.59; 97.91]	5.25 [1.44; 19.11]	0.15 [0.02; 0.95]	40.00 [19.12; 63.95]	77.78 [49.02; 92.72]	90.91 [61.11; 98.45]	85 [62.11; 96.79]
Gődény et al. 2016[13]	94.44 [72.71; 99.86]	65 [40.78; 84.61]	2.69 [1.47; 4.95]	0.08 [0.01; 0.59]	47.37 [30.98; 64.18]	70.83 [56.95; 81.68]	92.86 [65.32; 98.90]	78.94 [62.68; 90.45]
Ceylan et al. 2018[14]	76.92 [46.19; 94.96]	66.66 [29.93; 92.51]	2.30 [0.87; 6.09]	0.34 [0.12; 1.03]	59.09 [36.35; 79.29]	76.92 [55.80; 89.80]	66.67 [40.09; 85.67]	72.7 [49.78; 89.27]
Sherif et al. 2018[15]	83.33 [51.59; 97.91]	89.47 [75.20; 97.06]	7.91 [3.03; 20.69]	0.18 [0.05; 0.66]	24.00 [13.06; 38.17]	71.43 [48.88; 86.73]	94.44 [82.68; 98.37]	88 [75.69; 95.47]
Schroeder et al. 2020[16]	75 [42.81; 94.51]	76.92 [46.19; 94.96]	3.25 [1.14; 9.24]	0.32 [0.12; 0.91]	48.00 [27.80; 68.69]	75 [51.34; 89.51]	76.92 [54.48; 90.28]	76 [54.87; 90.64]
Park et al. 2020[17]	74.19 [61.50; 84.47]	44.44 [32.72; 56.64]	1.33 [1.04; 1.72]	0.58 [0.35; 0.95]	46.27 [37.62; 55.08]	53.49 [47.16; 59.71]	66.67 [54.94; 76.64]	58.2 [49.38; 66.67]
Sarma et al. 2021[18]	78.26 [56.30; 92.54]	85 [70.16; 94.29]	5.21 [2.42; 11.25]	0.25 [0.12; 0.56]	36.51 [24.73; 49.60]	75 [58.18; 86.61]	87.18 [75.60; 93.72]	82.53 [70.90; 90.95]
Linz et al. 2021[19]	83.33 [67.19; 93.63]	84.84 [76.24; 91.26]	5.5 [3.37; 8.96]	0.19 [0.09; 0.41]	26.67 [19.43; 34.96]	66.67 [55.10; 76.52]	93.33 [87.03; 96.69]	84.44 [77.21; 90.11]

PLR – positive likelihood ratio; NLR – negative likelihood ratio; PPV – positive predictive value; NPV – negative predictive value.

Discussion

Head and neck tumors are different types of oral cavity malignancies, including pharynx, larynx, nasal cavity, paranasal sinuses, and salivary glands. They can spread through several processes, including direct extension, hematogenous dissemination, perineural spread, and others. Perineural spread is the most dangerous of the above, as it allows metastasis of tumors through peripheral nerves, so its early detection is crucial to the patient's well-being and survival. The perineural spread can be seen with imaging tools.

The preferred methods for detecting perineural spread among head and neck tumors are MRI, CT, PET scan, among others. However, because of the high sensitivity and specificity of ^{18}F-FDG PET for cellular change and tumors, its use is highly recommended in various studies due to its high sensitivity in detecting perineural spread and recurrent metastatic tumors.[6–20] For example, Linz et al. reported the sensitivity of ^{18}F-FDG PET as 78.6% and specificity as 83.1%.[19] Similarly, Sherif et al. reported a high sensitivity of 83.33% and specificity of 89.47%.[15] Pyatigorskaya et al. reported a sensitivity of 90% and specificity of 98%.[22] Similar to the studies mentioned above, we achieved a high sensitivity of 91.7% and high specificity of 92.35%.

Apart from high sensitivity of ^{18}F-FDG PET, various studies reported its high accuracy; for example, in the study conducted by Tantiwongkosi, PET scanning has been deemed an accurate method and crucial initial step in identification and treatment planning of head and neck tumor.[23] Furthermore, Ng et al. reported its high accuracy of 98.4%, while Sherif et al. reported its accuracy of 88%.[6,15] Similarily, we obtained the accuracy of 91.5%. Based on these statistically significant results and high sensitivity, specificity and high diagnostic accuracy, this meta-analysis highly recommends using ^{18}F-FDG PET in predicting the perineural spread and in an accurate diagnosis of head and neck tumors.

Limitations

The limitation of the present study is the variability of PET instruments used and tests performed by different radiographers, which influences the risk of false negative results. Many studies reported comparable diagnosis of PNS with MRI, however,it's comparability with PET scan

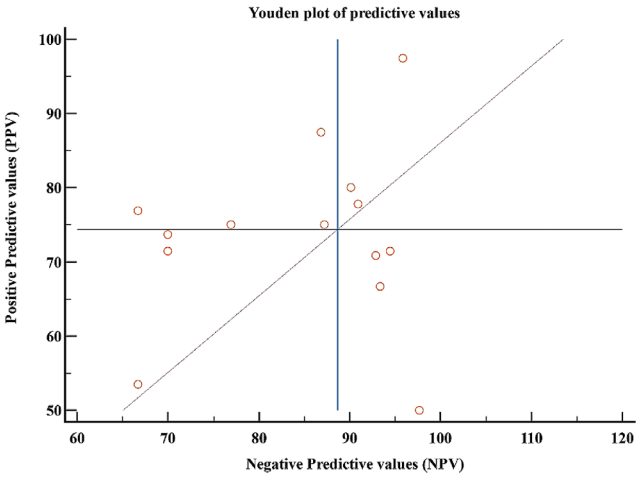

Fig. 6. Youden plot for predictive values

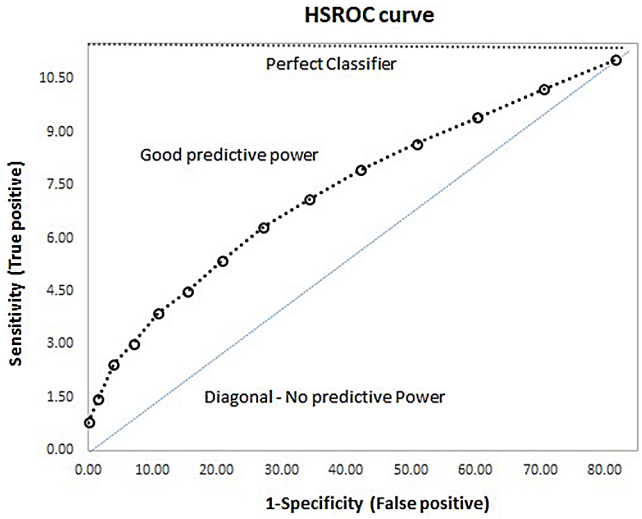

Fig. 7. Hierarchical summary receiver operating characteristic (HSROC) curve

in the diagnosis of PNS was not mentioned in the contemporary literature, so assessing the diagnostic comparability of MRI with PET scan accurately might affect the homogeneity of the data of the included studies. Data from other relevant studies showing the diagnostic accuracy of ^{18}F-FDG PET compared to other diagnostic imaging methods could also be included to support the role PET scan in the diagnosis of PNS. In order to reduce the variability among the data, detailed data on the patient's case history, physical examination and pathological tests could be included to further boost the diagnostic accuracy rate of ^{18}F-FDG PET in predicting perineural spread in head and neck tumors.

Conclusions

Magnetic resonance imaging is the gold standard for assessing perineural spread among head and neck tumors; still, ^{18}F-FDG PET is preferred chiefly as an effective imaging method due to its high sensitivity toward cellular change, perineural spread and early tumor detection rate. Furthermore, it is highly recommended since early detection can prevent metastasis and increase the chances of survival. In the current study, we analyzed the available related literature, and based on our statistically significant results, we highly recommend the use of ^{18}F-FDG PET to detect perineural spread among patients with head and neck tumors.

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